

Erythema Migrans Mimicking Cervical Cellulitis with Deep Neck Infection in a Child with Lyme Disease

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In the early stage of Lyme disease, atypical lesions of erythema migrans rash can develop and extend over the neck region, mimicking cervical cellulitis with deep neck infection. Here, we report a 9-year-old Taiwanese boy with a recent history of exposure to deer during his visit to Nanto County in central Taiwan. Cervical cellulitis with lymphadenitis was initially diagnosed. Erythema migrans developed in the following days and Lyme disease was finally diagnosed by a Western immunoblot test. Alertness to this unique clinical feature is required for prompt differential diagnosis of Lyme disease with a presentation of erythema migrans mimicking cervical cellulitis. [J Formos Med Assoc 2007;106(7):577–581]

Key Words: cervical cellulitis, childhood, erythema migrans, Lyme disease

Lyme disease is an emerging tick-transmitted human infection caused by the spirochetal agent *Borrelia burgdorferi*, and is recognized to be the most prevalent tick-borne illness worldwide.¹ The clinical manifestations of Lyme disease may involve multisystemic disorders, and the early stage of Lyme disease usually begins with an expanding skin rash known as erythema migrans (EM), which may occur in 60–80% of infected patients.² Treatment of early Lyme disease usually prevents the further progression of dermal lesions to the later syndromes of articular and neurologic complications. Although an adult case of Lyme borreliosis has been reported in Taiwan,³ pediatric case in native Taiwanese has never been documented. Thus, we report a 9-year-old Taiwanese boy who presented with an atypical lesion of expanding EM, which mimicked and was initially misdiagnosed as cervical cellulitis with deep cervical

infection. Laboratory tests led to the diagnosis of Lyme disease.

Case Report

A 9-year-old boy visited our pediatric clinic with the chief complaints of high fever, local redness, swelling, and painful sensation over the right side of his neck of 3 days' duration. Three months prior to the clinic visit, he had visited his grandfather's farm, and had deer contact, in Nanto County, central Taiwan, but he did not recall any history of a tick bite.

When he was admitted to our pediatric ward, he had a high-grade fever (rectal temperature, 39.6°C), a pulse rate of 120/minute, and blood pressure of 110/76 mmHg. Two tender masses (about 2.5 × 2.5 cm and 5 × 5 cm in size) with

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Received: March 10, 2006

Revised: June 19, 2006

Accepted: January 2, 2007

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local redness and swelling were noted over the right side of his neck. The general physical examination showed no other abnormalities. Cervical cellulitis with lymphadenitis was diagnosed initially.

Biochemical assays showed elevated C-reactive protein (CRP, 11.8 mg/dL) and white blood cell count ($10,100/\text{mm}^3$ with 85.8% neutrophils, 6.1% lymphocytes, 7.2% monocytes, 0.3% eosinophils). Complete blood count revealed a normal hemoglobin level (12.3 g/dL) and platelet count ($159,000/\text{mm}^3$). Rapid diagnostic tests for streptococcus antigen and other pathogenic agents by throat swab, throat culture, and bacterial cultures of blood revealed negative findings. Based on the observation of cervical lymphadenitis, neck computed tomography was performed and revealed multiple confluent lesions of enlarged nodes together with fat plane blurring extending from the right submandibular to the supraclavicular region. Deep cervical infection was suspected according to the imaging findings of suppurative lymphadenitis.

Empirical treatment with oxacillin was administered during the first 2 admission days, but intermittent high fever persisted. The erythematous skin rashes extended gradually from the right side to the left side of his neck and further disseminated to the chin, upper back, and anterior chest wall (Figure 1). The antibiotic treatment was shifted to ampicillin combined with sulbactam on the 3rd admission day. Elevated CRP (18.28 mg/dL) was noted on the 4th admission day. Moreover, bilateral knee arthralgia combined with myalgia was also noted on the 5th admission day. Due to the presentation of expanding skin rashes and history of recent exposure to deer, Lyme disease was suspected and a serum specimen was collected for testing. Doxycycline was added on the 6th admission day due to suspicion of Lyme disease and continued for 14 days, as previously recommended.⁴ The expanding skin lesions resolved completely within 3 days of starting doxycycline, and no articular disorder or neurologic impairment occurred. No signs of recurrence were observed at our pediatric clinic during the 3-year follow-up period.



Figure 1. Erythematous skin rashes (erythema migrans) extending gradually from the right side to the left side of the patient's neck. The skin lesion further disseminates to the chin, upper back, and anterior chest wall regions 3–5 days after admission.

Serodiagnosis for Lyme disease infection based on a two-step process recommended by the US Centers for Disease Control (CDC)⁵ was performed using indirect immunofluorescence assay (IFA) followed by Western immunoblot (WB) analysis using paired serum collected from the patient on the 6th and 20th admission days. The specimen collected on the 6th admission day yielded a positive IFA result with minor seroreactivities to the major *B. burgdorferi* antigens on WB analysis. Although the antibodies against *B. burgdorferi* could have been dampened by the doxycycline treatment, a comparative WB analysis with paired patient's serum collected on the 20th admission day revealed significant seroreactivities of IgG and IgM antibodies against the major protein antigens of various strains of *B. burgdorferi* (Figure 2A). In general, IgG Western blotting showed significant reactivities with the major antigens of 41, 45, 58, 63, 66 and 72 kDa protein bands. IgM Western blotting showed a strong reactivity with the 41 kDa and positive reactivities with the 45, 63, 66 and 72 kDa protein bands (Figure 2A). In contrast, serum from a negative patient revealed no seroreactive band against various strains of *B. burgdorferi* in the WB analysis (Figure 2B).

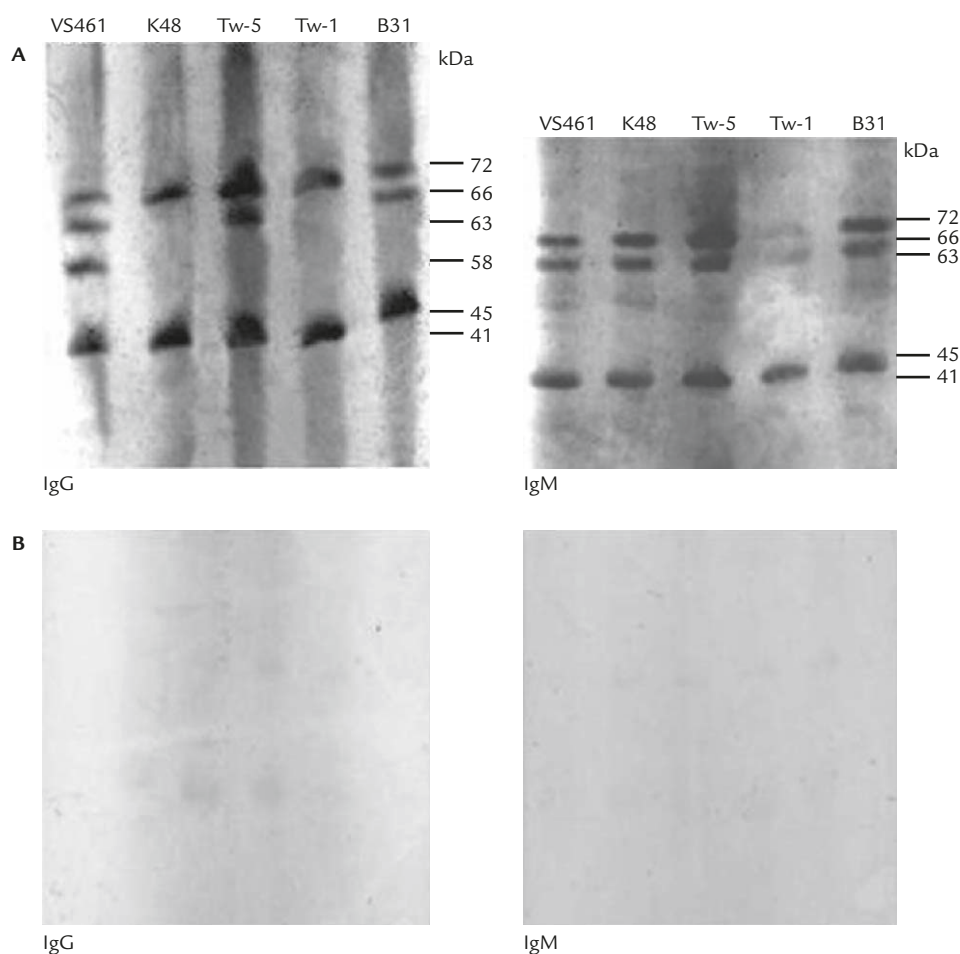


Figure 2. (A) A comparative Western immunoblot (WB) analysis with the patient's serum collected on the 20th admission day reveals significant seroreactivities of IgG and IgM antibodies against major protein antigens of various strains of *Borrelia burgdorferi*. (B) In contrast, a negative-diagnosed patient's serum reveals no seroreactive band in the WB test. Lane B31, American type strain B31; Lanes Tw-1 and Tw-5, Taiwan isolates TWKM1 and TWKM5, respectively; Lane K48, K48 isolate of *Borrelia garinii*; Lane VS461, VS461 isolate of *Borrelia afzelii*.

Discussion

Since the first adult case of Lyme disease had been documented in Taiwan,³ spirochetal isolates of Taiwan (designated as TWKM1-7) cultured from rodents provided solid evidence for the existence of Lyme disease spirochetes in the Taiwan area.⁶ As per our literature review, only one pediatric case of Lyme disease had been reported in Taiwan previously, and that case was an overseas Chinese girl who was born and lived in the United States, and she had traveled to visit her relatives in Taiwan.⁷ Thus, the present case with no travel history to any other countries is the first pediatric case of domestically acquired Lyme disease in Taiwan.

Early localized lesions of Lyme disease usually present as a solitary and gradually expanding EM rash with or without an influenza-like illness, and that may occur at the site of tick bite in 60–80% of infected persons.² A study of Lyme disease in

children, however, indicated that the head or neck region was the most common site of single EM lesion, and that only 36% of infected children with an EM lesion had a recognized tick bite within the preceding month.⁸ Indeed, our patient who presented with an expanding EM lesion over the neck region is compatible with the previous descriptions of pediatric Lyme disease.

Influenza-like symptoms of headache, arthralgia, fever, and regional lymphadenopathy may present as early manifestations of Lyme disease infection.⁸ A previous study also reported that 23% of patients with culture-confirmed early Lyme disease presented with localized lymphadenopathy,⁹ and this clinical feature may serve as a marker of early Lyme disease prior to the appearance of characteristic EM rash and disseminated symptoms.¹⁰ Indeed, our patient also presented with localized heating rash combined with cervical lymphadenitis prior to the development of

well-differentiated and progressively expanding EM. These features should remind pediatricians to keep on the alert for the possible manifestations of Lyme disease characterized by regional lymphadenitis combined with local inflammatory rash, especially at the cervical region.

According to the criteria recommended by the US CDC, the diagnosis of Lyme disease is defined by the appearance of EM rashes (> 5 cm in diameter) or at least one of the clinical manifestations of musculoskeletal, neurologic or cardiovascular disease, combined with serologic evidence of elevated IgG or IgM antibodies against *B. burgdorferi*.^{5,11} Although cultivation of *B. burgdorferi* from the patient's tissue by Barbour-Stoenner-Kelly (BSK) medium may also provide definitive diagnosis, the yield from this *in vitro* culture is time-consuming and the sensitivity is too low for it to be a practical method for clinical diagnosis.¹² In contrast, Western immunoblot test can detect the elevated antibodies against *B. burgdorferi* in a serum specimen even after successful treatment. This technique is also used to confirm equivocal and positive results tested by ELISA or IFA.¹¹ Thus, serodiagnosis has been adopted as a standard diagnostic method in public health surveillance and in clinical confirmation of Lyme disease.

The differential WB banding in infected patients is attributed to the variable seroreactivity of patients' serum against *Borrelia* protein antigens. Regardless of the two-test approach criteria recommended by the US CDC,^{5,11} a positive diagnosis suggested by the European Union Concerted Action on Lyme Borreliosis (EUCALB) requires only two seroreactive bands among 10 major *Borrelia* protein antigens for IgG WB, and only one seroreactive band among three major *Borrelia* protein antigens (39 kDa, 23 kDa, and 17 kDa) or a strong 41 kDa band for IgM WB.¹³ In addition, previous study on the frequency of WB reactivity to specific *Borrelia* protein antigens also revealed that the seroreactivity of IgG antibody against the higher molecular weight bands (41 kDa and above) was most frequently detected in infected patients.¹⁴ Indeed, the present case also showed significant seroreactivities of IgG and IgM antibodies against

the higher molecular weight bands of *Borrelia* antigens (Figure 2A). In contrast, no band was observed in a negative-diagnosed patient's serum (Figure 2B). Thus, a positive-diagnosed patient's serum may reveal various banding patterns according to the differential seroreactivity of individual patients against *Borrelia* protein antigens.

Practice guidelines for the treatment of Lyme disease have been recommended by the Infectious Disease Society of America, and doxycycline for a course of 14–21 days is suggested as the first-line choice for the treatment of patients older than 8 years of age.⁴ The prognosis is excellent for pediatric cases of early Lyme disease treated promptly with a conventional course of antimicrobial agents. As in our patient, the main symptoms including fever, skin lesions, arthralgia, and myalgia resolved within 3 days of treatment with doxycycline. There were no recurrent signs of skin lesions, and no articular or neurologic complications were observed during the 3-year follow-up.

In conclusion, we reported a laboratory-confirmed pediatric case of Lyme disease in a 9-year-old Taiwanese boy who presented with an atypical progressively expanding EM lesion, which was initially misdiagnosed as cervical cellulitis. This rare feature should remind pediatricians to consider Lyme disease in the differential diagnosis of pediatric patients with cervical cellulitis.

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